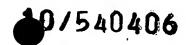
Rec'd 1 PTO 24 JU 2005

PATENT COOPERATION TREATY 0/540406

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference				FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)								
International application No. PCT/EP2004/000729				International filing date (day/month/year) 28.01.2004				Priority date (day/month/year) 29.01.2003				
	nation 'H21		ent Classification (IPC) or b	oth national classification	and IPC		Roc Par ASK BK	tent l	Diagnos Departme U. NOV	nt Penz	mbH berg WN	·
Appli RO(DIAG	SNOSTICS GMBH.et.	al.			ВИЯ	НН	HIL	М	+	eraseau e en de c
1.	This Auti	s inter hority	national preliminary exar and is transmitted to the	nination report has be applicant according to	en prepar Article 3	red by 6.	this I	nterr	national F	Prelimir	nary E	xamining
2.	This	REP	ORT consists of a total of	of 5 sheets, including	this cover	sheet	t. '	-				
	⊠	bee (see	report is also accompain amended and are the less Rule 70.16 and Section	basis for this report an a 607 of the Administra	d/or sheet	ts con	tainin	g red	ctification	and/or s made	drawi e befo	ngs which have re this Authority
	ine	se an	nexes consist of a total of	of 2 sneets.								
3. .		•	rt contains indications re	lating to the following i	tems:				 ,		,	
	l II	\boxtimes	Basis of the opinion Priority									
	Ш		•	ppinion with regard to i	novelty, in	ventiv	e ste	p an	d industr	ial appl	icabili	ty
	III □ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV □ Lack of unity of invention											
	٧	M	Reasoned statement u citations and explanation	nder Rule 66.2(a)(li) wons supporting such st	ilth regard	d to no	velty	, inve	entive ste	p or in	dustria	al applicability;
	VI		Certain documents cité	d								
	VII		Certain defects in the in	• •								
	VIII	LI.	Certain observations of	n the international app	lication			-				
												•
Date o	of sub	missio	n of the demand		Date of	comple	tion o	f this	report			
09.06	09.06.2004			29.11.2004								
Name	Name and mailing address of the international preliminary examining authority:				Authorized Officer							
	116	Eur	opean Patent Office 0298 Munich		Honn-	-d ^						
Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465				Hennard, C								
					Telephone No. +49 89 2399-7355							



JC20 Rec'd PCT/PTO 2 4 JUN 2005

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2004/000729

	D		- 4	AL -		
I.	Bas	:IS	ОТ	tne	report	•

1. With regard to the **elements** of the international application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)):

	De	scription, Pages						
1-26			as originally filed					
er, i	Cla	ims, Numbers	s for the state of the same of					
	1-1	4	received on 07.09.2004 with letter of 03.09.2004					
Drawings, Sheets								
	1/14	1-14/14	as originally filed					
2.	Wit lan	h regard to the language guage in which the intern	e, all the elements marked above were available or furnished to this Authority in the ational application was filed, unless otherwise indicated under this item.					
	The	ese elements were availa	ble or furnished to this Authority in the following language: , which is:					
		the language of a transl	ation furnished for the purposes of the international search (under Rule 23.1(b)).					
		the language of publicat	tion of the international application (under Rule 48.3(b)).					
		the language of a transl Rule 55.2 and/or 55.3).	ation furnished for the purposes of international preliminary examination (under					
3.	Witi inte	n regard to any nucleoti on rnational preliminary exa	de and/or amino acid sequence disclosed in the international application, the mination was carried out on the basis of the sequence listing:					
		contained in the internal	tional application in written form.					
		filed together with the in	ternational application in computer readable form.					
☐ furnished subsequently to this Authority in written form.								
☐ furnished subsequently to this Authority in computer readable form.								
		The statement that the sin the international appli	subsequently furnished written sequence listing does not go beyond the disclosure cation as filed has been furnished.					
		The statement that the illisting has been furnished	nformation recorded in computer readable form is identical to the written sequence ed.					
4.	The	amendments have resul	Ited in the cancellation of:					
		the description, page	ges:					
		the claims, No	s.:					
		the drawings, she	eets:					

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2004/000729

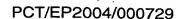
5. 🗆	This report has been established as if (some of) the amendments had not been made, since they hat been considered to go beyond the disclosure as filed (Rule 70.2(c)).						
	(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)						

- 6. Additional observations, if necessary:
- V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	None
Inventive step (IS)		Claims Claims	1-14 None
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	None

2. Citations and explanations

see separate sheet



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1. The following documents have been used in the evaluation of the present application:
 - D1: NUCLEIC ACIDS RESEARCH, vol. 29, no. 13, 2001, pages e65-1-e65-7
 - D2: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 92, no. 3, 1970, pages 724-726
 - D3: ANALYTICAL BIOCHEMISTRY, vol. 226, 1995, pages 161-166
 - D4: THE JOURNAL O BIOLOGICAL CHEMISTRY, vol. 257, no. 9, 1982, pages 4796-4805
 - D5: BIOTECHNIQUES, vol. 33, no. 3, September 2002, pages 526-531
 - D6: NUCLEIC ACIDS RESEARCH, vol. 22, no. 4, 1994, pages 695-696
 - D7: NUCLEIC ACIDS RESEARCH, vol. 26, no. 21, 1998 pages 5009-5010
 - D8: NUCLEIC ACIDS RESEARCH, vol. 22, no. 15, 1994, pages 2990-2997
 - D9: US-A-4 844 880

2. Novelty (Article 33(2) PCT):

The claimed subject-matter of the newly filed claims 1-14 of the present application are not disclosed in the documents cited and is therefore considered novel. These claims fulfil the requirements of article 33(2) PCT.

3. Inventive merit (Article 33(3) PCT):

D1, which is considered to be the closest prior art, concerns the transformation of cytosine into uracil using various operating conditions involving bisulphite as a reactant (see page e65-2, "deamination"; page e65-3, table 1 and last paragraph). In particular, this document describes the bisulphite reaction at 80 and 85 degrees Celsius during 1 and 4 hours (among others) and using bisulphite concentrations between 3.87 - 4.26 M or between 5.20 - 5.69 M at pH 5.0. This document also clearly teaches that by increasing the reaction temperature, the full conversion is achieved in a shorter time.

The method of the application distinguishes itself from **D1** by the reacting time which is between 1.5 and 3.5 hours.

From the comparative tests provided by the applicant (with letter of 13.10.2004) it appears that the technical effect achieved by selecting a reaction time between 1.5 and 3.5 hours using the concentration, pH and temperature as defined in **claim 1** is that a higher transformation yield is obtained.



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

PCT/EP2004/000729

The problem to be solved by the present application can therefore be formulated as to find a method to transform cytidine into uracil with better yield.

The solution suggested by the present application is therefore an alternative to **D1**. The comparative example presented in the tests of 13.10.2004 demonstrate the unexpected effect that the combination of the specific conditions (concentration of bisulfite, pH, temperature and reaction time) give a higher transformation yield.

Due to this unexpected result, an inventive merit can be recognised in the method of claim 1 which thus fulfills the requirements of article 33(3) PCT.

The optimised conversion conditions being obtained by the combination of the appropriate concentration of bisulfite, pH and the temperature, the use of such a solution for the conversion of cytosine to uracil (claim 8) as well as the kit (claim 11) and the solution (claim 12) claimed are also considered to demonstrate an inventive merit over the prior art.

It is concluded that claims 1-14 of the present application fulfil the requirements of article 33(3) PCT.

4. Industrial applicability (Article 33(4) PCT):

Due to the nature of the claims, an industrial applicability of the invention is obvious and claims 1-14 are considered to fulfil the requirements of Article 33(4) PCT.